

Neonatal Thrombocytopenia

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Thrombocytopenia

Definition

- Platelet count $<150,000$ (1-2% of healthy term infants)
 - Mild 100-150,000
 - Moderate 50-99,000
 - Severe $<50,000$
- (Less than 5% of infants <32 weeks have platelets $<104,000$ and in late preterm $<123,000$)

Incidence

- ~18-32% of infants admitted to NICU develop thrombocytopenia during their stay.
- Increased frequency in more preterm infants.
- Increased risk for ICH, mortality, and long term neurodevelopmental disability.

Platelet production

4 steps

1. Production of Thrombopoietin (Tpo)
 2. Proliferation of megakaryocytes progenitors
 3. Megakaryocyte maturation
 4. Development and release of new platelets.
- Platelet production starts at the end of the first trimester of pregnancy.
 - There are measures of platelet production such as serum Tpo or reticulate platelet percentages (RP%) but they are not reliable in infants.

Differential Diagnosis

Table 1.

	Condition
Fetal	Alloimmune Congenital infection (e.g. CMV, toxoplasma, rubella, HIV) Aneuploidy (e.g. trisomies 18, 13, 21, or triploidy) Autoimmune (e.g. ITP, SLE) Severe Rh haemolytic disease Congenital/inherited (e.g. Wiskott-Aldrich syndrome)
Early onset neonatal (<72 hours)	Placental insufficiency (e.g. PET, IUGR, diabetes) Perinatal asphyxia Perinatal infection (e.g. <i>E coli</i> , GBS, <i>Haemophilus influenzae</i>) DIC Alloimmune Autoimmune (e.g. ITP, SLE) Congenital infection (e.g. CMV, toxoplasma, rubella, HIV) Thrombosis (e.g. aortic, renal vein) Bone marrow replacement (e.g. congenital leukaemia) Kasabach-Merritt syndrome Metabolic disease (e.g. propionic and methylmalonic acidemia) Congenital/inherited (e.g. TAR, CAMT)
Late onset neonatal (>72 hours)	Late onset sepsis NEC Congenital infection (e.g. CMV, toxoplasma, rubella, HIV) Autoimmune Kasabach-Merritt syndrome Metabolic disease (e.g. propionic and methylmalonic acidemia) Congenital/inherited (e.g. TAR, CAMT)
The most common conditions are highlighted. CMV, Cytomegalovirus; ITP, idiopathic thrombocytopenic purpura; SLE, systemic lupus erythematosus; PET, pre-eclampsia; IUGR, intrauterine growth restriction; <i>E coli</i> <i>Escherichia coli</i> ; GBS, group B streptococcus; DIC, disseminated intravascular coagulation; TAR, thrombocytopenia with absent radii; CAMT, congenital amegakaryocytic thrombocytopenia; NEC, necrotising enterocolitis.	

Neonatal thrombocytopenia: causes and management.
 Roberts I; Murray NA

Archives of Disease in Childhood Fetal & Neonatal Edition. 88(5):F359-64, 2003 Sep.

Table 1. Classification of fetal and neonatal thrombocytopenias

Early Onset <72 hrs

- Well Appearing: Most common is autoimmune thrombocytopenia or placenta insufficiency (PIH or chronic HTN)
 - Mild to moderate thrombocytopenia
 - Nadir on postnatal day 4-5
 - Usually resolves by 7-10 days.
- More severe NAIT
- Ill Appearing: Sepsis (Bacterial or viral), TORCH, DIC

Neonatal Autoimmune Thrombocytopenia

- Early onset, moderate-severe thrombocytopenia
- Usually a maternal history of ITP or autoimmune disease (2 in 1000 pregnancies)
- Any infant born to a mom with autoimmune disease should have a platelet count (incidence is about 10%).
- Can treat with IVIG for thrombocytopenia, may need platelet transfusion.
- Evaluate for ICH (incidence is ~1%).
- Can last from days to months.

Neonatal Alloimmune Thrombocytopenia (NAIT)

- Severe thrombocytopenia ($<50,000$)
- Increased risk for ICH (Incidence is 8-22%)
- May present antenatally with ICH, severe hydrocephalus, hydrops fetalis.
- Incidence 1 in 1500 pregnancies
- Due to maternal Ab to paternal Ag
- Can occur in first pregnancy
- Testing of Mother and Father for Human Platelet antigen (HPA) 1, 3, and 5. (90% of cases)

Neonatal Alloimmune Thrombocytopenia (NAIT)

- If platelets <50,000- Suggest cerebral imaging (US,CT,MRI)
- Transfuse platelets:
 - trial of random donor platelets first.
 - If ineffective: Antigen negative platelets should be used (maternal platelets or known PL A1 or PL A5 negative platelets)
- Consider IVIG 1g/kg q 24hrs x 2 doses (can be given to help patient increase own platelets or in combination with random donor transfusions.
- Consider methylprednisolone (1mg/kg q 8hrs) with IVIG.

Neonatal Alloimmune Thrombocytopenia (NAIT)

- Usually resolves within 2 weeks
- But platelet count needs to be followed until normalized and stable.
- If persists longer may be a different diagnosis.
- Monitoring for future pregnancies and possibly treatment with maternal IVIG/steroids.

Late-Onset Thrombocytopenia

- Ill Appearing: Sepsis, NEC, IEM (Propionic Acidemia, isovaleric acidemia, methylmalonic acidemia, Gaucher Disease)
- Well Appearing: Drug induced, thrombosis, Fanconi's Anemia

Physical Exam

- Ill or Well
- Petechia, bruising
- Fontonelle
- Liver size
- Abdominal masses (renal vein thrombosis)
- Dysmorphic features
- Forearm or thumb abnormalities (TAR syndrome or Fanconi anemia)

Genetic Disorders Associated With Thrombocytopenia

- From Neoreviews 2009

- **Chromosomal:** Trisomy 13
Aplasia cutis, CHD, cleft lip and palate, polydactyly
- Trisomy 18
IUGR, CHD, rocker-bottom feet, overlapping digits, hypertelorism, small mouth, clinodactyly
- Trisomy 21
CHD, single palmar crease, hypotonia, short neck, w/ redundant posterior folds
- Turner syndrome
CHD, cubitus valgus, webbed posterior neck, broad chest, with wide-spaced nipples, lower extremity edema
- 11 q terminal disorder (Jacobsen syndrome)
CHD, GU anomalies, facial anomalies, abnl brain imaging, limb anomalies
- **Familial :** May-Hegglin anomaly
(Sebastian syndrome)
Giant platelets, neutrophilic inclusions
- Fechtner syndrome
Giant platelets, sensorineural hearing loss, cataracts, nephritis, neutrophilic inclusions
- Bernard-Soulier syndrome
Anemia, genitourinary abnormalities (cryptorchidism)
- Congenital amegakaryocytic thrombocytopenia
Abnl head size and shape, developmental delay, CHD, cleft and high-arched palate, abnormal kidneys, optic atrophy, valgus and varus deformities, vertebral anomalies, coloboma, scoliosis, absent bone marrow megakaryocytes
- Wiscott-Aldrich syndrome
Immunodeficiency, small platelets, eczema
- Amegakaryocytic **thrombocytopenia**
Restricted forearm pronation, proximal radioulnar synostosis in forearm, and radioulnar synostosis absent bone marrow megakaryocytes
- Fanconi anemia
Hypopigmented and hyperpigmented skin lesions, urinary tract abnormalities, microcephaly, upper extremity radial-side abnormalities involving the thumb, pancytopenia (usually with onset in childhood)
- Thrombocytopenia and absent radii
Shortened/absent radii bilaterally, nml thumbs, ulnar and hand abnormalities, abnormalities of the humerus, CHD, eosinophilia, leukemoid reaction
- Neonatal primary hemophagocytic lymphohistiocytosis
Fever, HSM, hyperferritemia, hypertriglyceridemia, hypofibrinogenemia
- **Metabolic:**
- Propionic acidemia, methylmalonic acidemia
FTT, developmental delay, ketoacidosis, hyperglycinemia, hyperammonemia
- Isovaleric acidemia
Odor of sweaty feet, poor feeding, hypotonia, hyperammonemia, metabolic acidosis
- Gaucher disease
Hepatosplenomegaly, Gaucher cells in bone marrow

Management

- Any doubt repeat sample
 - Errors from improper collection or unrecognized platelet clumping
- Blood culture +/- antibiotics depending on history, clinical picture and severity.
- Review peripheral smear and MPV (Jacobsen and Fechtner syndromes present with large platelets and Wiskott-Aldrich syndrome and X-linked thrombocytopenia present with small platelets)

Management

- Transfuse platelets: (volume reduction not necessary)
 - $<30,000$ - if clinically stable term or preterm > 1 week of age and no ICH
 - $<50,000$ for ill term infants or preterm infants (<33 weeks) in the first week of age.
 - $<100,000$ if ICH or signs of active bleeding.
- Andrew et al 1993 showed preterm infants tx at $< 150,000$ vs $<50,000$ no differences in freq or severity of ICH
- Murray et al 2002 retrospective review no major hemorrhage in infants if platelets $>30,000$.

Management

- 10-15ml/kg random-donor platelets
 - Either CMV neg or leukoreduced
 - Irradiation to reduce GVHD
- Platelet transfusions associated with TALI and increased mortality
- If neonate responds to transfusion:
 - But needs transfusions on a weekly basis more likely due to decreased platelet production (congenital amegakaryocytic thrombocytopenia)
 - If needed every 1-2 days more likely increased platelet consumption.

References

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